

## *Depression and end-of-life care for patients with cancer*

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*Patients with cancer and depression experience more physical symptoms, have poorer quality of life, and are more likely to have suicidal thoughts or a desire for hastened death than are cancer patients who are not depressed. Despite the ubiquity of depressive symptoms in cancer patients at the end of life, critical questions remain unanswered with respect to etiopathogenesis, diagnosis, and treatment of depression in these vulnerable patients. The pharmacotherapy of depression in patients with advanced cancer should be guided by a palliative care approach focused on symptom reduction, irrespective of whether the patient meets diagnostic criteria for major depression. Earlier and more intensive supportive care for patients with cancer reduces symptom burden and may prolong life for patients with advanced disease. Symptom-oriented clinical trials are needed to improve end-of-life cancer care.*

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### Background

**D**epression occurs commonly, but not inevitably, in patients with cancer at the end of life. Although there are over 7 million cancer deaths around the world each year,<sup>1</sup> estimates of the prevalence of depression in terminally ill cancer patients are imprecise. Most studies of comorbid cancer and depression either make no distinction between cancer phases (eg, newly diagnosed, active treatment, survivorship, stable metastatic disease, end-stage) or fail to operationally define “end-of-life” care. Consequently, reported prevalence rates for depression in patients with cancer span a broad range. Best estimates are that between 15% and 50% of cancer patients experience depressive symptoms, and 5% to 20% will meet various diagnostic criteria for major depressive disorder.<sup>2-7</sup>

Similarly, few data are available with respect to the frequency with which cancer patients are appropriately treated for depression at the end of life.<sup>8,9</sup> Only a small number of controlled clinical trials have been conducted with depressed cancer patients, whether or not they are in a terminal phase of their illness. Accordingly, the scope and magnitude of suffering due to unrecognized and inadequately treated depression in terminally ill cancer patients remains both unknown and unfortunate.

Research findings on end-of-life cancer care do not paint an entirely bleak picture. Incurable cancer represents the

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paradigmatic existential crisis and thus an opportunity for individual reflection and interpersonal communion. Several promising lines of investigation have demonstrated the benefits of meaning-oriented psychological therapies and palliative care interventions on quality, and perhaps duration, of life for end-stage cancer patients.<sup>10-13</sup> Taken together, these data suggest two important conclusions: (i) despite the widely held sentiment that depression is both an unavoidable and “appropriate” response to the dying process, most terminal cancer patients do not meet diagnostic criteria for major depression but can still benefit from medical and psychosocial interventions; and (ii) depressive symptoms, when they do complicate terminal cancer care, warrant accurate diagnosis and aggressive treatment to reduce the substantial suffering of these patients.

This article reviews several ways in which depression impacts end-of-life care for adults with cancer. Specific topics include the diagnosis of depression in seriously ill cancer patients; the co-occurrence of depression and somatic symptoms; the impact of depression on the course of illness; depression and decision-making capacity; suicide; desire for hastened death; treatment of depression in patients with advanced cancer; and recent research in palliative care that is relevant to depression at the end of life.

## Diagnosis of depression in patients with advanced cancer

Optimum end-of-life care for cancer patients requires an ability to make an accurate diagnosis of depression. The frequency with which depression is both underdiagnosed (eg, dismissed as a normal and anticipated response to illness or not considered at all) and misdiagnosed (eg, mistaken for delirium or poorly controlled pain) in the oncology setting is a manifestation of the clinical complexity of patients dying from cancer.<sup>14</sup> The patient with widely metastatic cancer who is enduring chemotherapy and radiation treatment is more likely than not to experience sleep disturbance, fatigue, anorexia, and weight loss, whether a depressive syndrome is present or absent. Whereas the failure to recognize depression can result in needless suffering, misdiagnosis can cause avoidable harm by means of inappropriate pharmacological treatment. The most frequent and consequential example of this diagnostic and pharmacological mismanagement is delirium. Hypoactive delirium is the most common subtype of delirium, and particularly likely to be mistaken

for depression.<sup>15-21</sup> Prescribing an antidepressant or a psychostimulant to a patient who is withdrawn as a result of delirium, rather than depression, is more likely to exacerbate the delirium than alleviate depressive symptoms. Avoiding this common clinical error is particularly important for the terminal cancer patient, as the prevalence of delirium can approach 90% in the final days before death.<sup>17,22,23</sup> For some clinicians, it is tempting to view the relatively calm, confused state of hypoactive delirium as a desirable way to die. However, delirium at the end of life can be deeply distressing to patients, family members, and caregivers.<sup>24,25</sup> Terminal delirium also interferes with a patient’s ability to participate in their care and say goodbye to loved ones.

Chemotherapy and other medications used in cancer treatment (eg, glucocorticoids, narcotics, benzodiazepines, antihistamines, and antibiotics) often lead to adverse effects that mimic depression. Notably, dopamine-blocking antiemetics such as metoclopramide (Reglan), prochlorperazine (Compazine), and promethazine (Phenergan) cause akathisia, which may in turn be misdiagnosed as an anxious or agitated depression.<sup>26,27</sup> Clinicians are thus faced with the task of differentiating somatic symptoms that masquerade as depression from a superimposed syndromal depression that complicates the course and treatment of cancer. Not surprisingly, even experienced psycho-oncologists struggle with this difficult determination.

Even when physiological and pharmacological mimics of depression have been ruled out, clinicians confront several additional diagnostic dilemmas. Dying patients can experience a broad spectrum of depressive symptoms, ranging from transient sadness to psychotic depression. In contrast to the countless studies of depressive phenomenology in patients without medical comorbidity, there has been little research in the oncology setting to help clinicians distinguish between major depressive disorder, adjustment disorder with depressed mood, mood disorder due to a general medical condition, pathological grief, demoralization, and subsyndromal depressive symptoms.<sup>28-31</sup>

Given this diagnostic complexity, it is therefore not surprising that estimates of depression in the oncology setting vary so widely. It is likely that the prevalence of major depressive disorder increases with advanced stages of cancer<sup>3,4</sup> and varies by tumor site.<sup>32,33</sup> However, all cancer types are associated with a rate of depression that is significantly higher than the general population.

## Depression, somatic symptoms, and course of cancer

Patients with terminal cancer suffer from an enormous symptom burden. A recent review of 44 studies, including data from thousands of patients, estimated symptom prevalence in individuals with incurable cancer.<sup>34</sup> Five symptoms (fatigue, pain, lack of energy, weakness, and appetite loss) were reported in greater than 50% of patients. The prevalence of nervousness and depression were 48% and 39%, respectively. As described earlier, many of the core diagnostic symptoms of depression are precisely those symptoms experienced most commonly by cancer patients at the end of life.<sup>34</sup> Importantly, somatic symptoms frequently co-occur with depression in cancer patients and are associated with increased disability.<sup>35</sup>

It is now well-established that depression is an independent predictor of mortality in patients with coronary heart disease.<sup>36</sup> Could a similar effect of depression be true for patients with cancer as well? A meta-analysis by Satin and colleagues<sup>37</sup> published in 2009 suggests that depression may predict mortality in cancer patients. Out of 9417 patients, those with depressive symptoms had a 26% greater mortality, and those diagnosed with major depressive disorder had a 39% higher mortality, an effect that was independent of other risk factors. In a retrospective cohort study of women with breast cancer, Danish investigators observed a modest, cancer phase-dependent increase in mortality in women who had preoperative or postoperative depression.<sup>38</sup> A smaller retrospective study of patients with malignant brain astrocytomas found that preoperative depression was independently associated with decreased survival at 12 and 20 months.<sup>39</sup> To be sure, these observations require confirmation in larger, prospective studies. Furthermore, even if a negative prognostic effect of depressive symptoms is established for cancer, it will need to be demonstrated that the early detection and successful treatment of depression positively impacts survival. Until then, the most compelling rationale for depression screening and treatment remains the clinical imperative to relieve suffering and improve functioning.

## Depression and decision-making

Modern cancer care presents patients with challenging decisions that begin with screening tests (eg, serum prostatic specific antigen levels, BRCA1 status) and con-

tinue through end-of-life care. As death approaches, patients and their caregivers are frequently faced with treatment options that hold diminishing chances of benefit and escalating likelihood of toxicity. Making these choices is particularly difficult when decision-making is colored by physical discomfort, existential fear, or depression. Not surprisingly, a patient's decision to discontinue active cancer treatment is a common trigger for psychiatric assessment of depression.

Basic components of decision-making capacity (DMC) include knowledge, intellectual skills, memory, attention, concentration, conceptual organization, and aspects of "executive function" such as the ability to plan, solve problems, and make probability determinations. Most of the psychiatric literature on DMC is focused on these cognitive functions and employs psychometric approaches to the study of subjects with neuropsychiatric illnesses such as dementia, psychosis, major depression, and bipolar disorder.<sup>40-42</sup> In contrast, the contributions of mood, motivation, faith, and other influences on risk assessment and decision-making have received less attention but have clear implications for end-of-life care. The extent to which these factors, and less easily quantified concepts like intuition, trust, or ambivalence affect the decision-making process is not known. Much work remains to be done to better understand these other determinants of decision-making; however, it is clear that focusing on cognitive impairment to the exclusion of mood effects is shortsighted.

Depression is more likely to influence or compromise a patient's decision-making abilities than it is to render them incapacitated or legally incompetent.<sup>42-46</sup> Competence and DMC are closely related but distinct constructs.<sup>47</sup> In most developed countries, adults are presumed legally competent to make autonomous decisions unless a formal judgment of legal incompetence is rendered. Competence determinations are typically based on the ability to make specific decisions at a given point in time (eg, choices concerning medical care, management of finances, designation of a substitute decision-maker, execution of a will). Standards for determining competence vary by jurisdiction but are based in large part on clinical assessments of an individual's cognitive state and DMC. From a legal perspective, a person is either competent to make decisions for themselves or incompetent to do so, in which case someone else makes decisions on their behalf. As a practical matter, dying patients are infrequently subjected to formal legal competency evaluations. Exceptions may arise

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when family members feel that a patient is not able to make medical or financial decisions. More commonly, clinical judgments are used to assign decision-making authority when patients become incapacitated. Silvera and colleagues found that more than a quarter of elderly patients followed in a longitudinal study required surrogate decision-making at the end of life and that having executed an advance directive significantly influenced outcomes.<sup>48</sup>

A frequently observed phenomenon in end-of-life cancer care is the differential threshold for concern about DMC, depending on the degree to which the patient is adherent to medical recommendations. Patients who refuse a diagnostic or therapeutic procedure are often suspected of having impaired DMC. In contrast, decisionally impaired patients who are passive and agreeable with requests from their caregivers rarely engender these same concerns. As described above, the diagnosis of hypoactive delirium is often missed or not appropriately treated at the end of life. One of several reasons to diagnose and aggressively treat delirium (with or without agitation) is that it may restore DMC and thus allow patients to make important medical decisions for themselves.<sup>49</sup>

In summary, depression produces more subtle distortions in DMC than delirium or psychosis, but refusal of even life-prolonging treatment by a depressed patient cannot not be assumed to constitute either suicidality or lack of competence.<sup>43,50</sup> Consequently, patients should be strongly encouraged to accept treatment for depression, but a decision to override a refusal of medical treatment should be based on a formal assessment of DMC rather than solely on the basis of depression.

## Cancer and suicide

The association between cancer and suicidal behavior is neither novel nor surprising. Although it appears that the absolute numbers of suicides in cancer patients is low, cancer patients clearly have an elevated relative risk of both suicidal ideation and completed suicide as compared with both the general population and patients with other medical illnesses. Depression, pain, debility, hopelessness and a sense of being a burden to others have been identified as key risk factors for suicidal behavior.<sup>51,52</sup> Recently, investigators have queried large databases and employed sophisticated methodology to study this important clinical problem. These data suggest that the suicide rate for persons with cancer is at least twice the rate observed in the general US population.<sup>53-55</sup>

Specific patterns of suicide have emerged from these studies that have direct clinical relevance. There is a differential risk of suicide depending on gender and cancer type, with prostate, gastrointestinal, head and neck, and lung cancers associated with higher rates.<sup>55-58</sup> Suicide also tends to be more frequent within the first months after diagnosis and soon after discharge from the hospital.<sup>59,60</sup> Consequently, the ability to assess depression and suicide risk should be considered a core competency for clinicians who work with cancer patients. This is particularly important since oncology clinicians are often unable to identify depression and other factors that put their cancer patients at higher suicide risk, and only a minority of cancer patients are appropriately referred to mental health professionals.<sup>14,61,62</sup>

## Desire for hastened death

Few clinical scenarios generate a request for psychiatric evaluation more predictably than when a patient expresses a wish to die. Walker et al<sup>63</sup> reported results from over 3000 patients screened for suicidal ideation in an outpatient oncology clinic in Edinburgh, Scotland. Eight percent of patients endorsed thoughts of being better off dead or having thoughts of hurting themselves in some way. This communication can be an expression of countless thoughts and feelings including the following: a passive wish to be free of suffering; a worry about future pain; an expression of need for control; a specific plan to commit suicide; a rejection of futile life-sustaining treatments (withdrawal of care); an acceptance of death; an elicitation of help in ending one's life (physician-assisted suicide); or a request to be killed (euthanasia).<sup>31,64-69</sup> Under any circumstances, an endorsement of suicidal ideation or a request for an intentionally arranged death is an expression of distress that warrants careful clinical assessment.

Muskin<sup>68</sup> observed that physicians respond to requests to die by focusing predominantly on determinations of the patient's DMC. He argued persuasively that too often there is inadequate attention to the underlying meaning and importance of these requests. Whereas competent subjects have the right to refuse life-sustaining treatments (and in Oregon and Washington in the US, as well as in Belgium, Luxembourg, and Switzerland, request physician-assisted suicide), a compassionate and comprehensive psychiatric evaluation can help clarify both the patient's concerns and the ethically permissible medical options.

## Treatment of depression in end-of-life cancer care

Treatment guidelines for major depression in otherwise medically healthy patients are well established and include an impressive array of pharmacological and psychotherapeutic interventions. Whether these same treatments are as effective for patients with cancer, especially those with end-stage cancer, is not known. Psychosocial interventions for depressed cancer patients have been more extensively studied than psychopharmacological treatments. Several psychological interventions have been either adapted or designed specifically for patients with cancer. A recent Institute of Medicine report on psychosocial care of cancer patients provides a comprehensive and critical review of these treatments.<sup>70</sup> Of particular promise are interventions that employ principles of existential psychology and meaning-centered life review,<sup>10,12</sup> collaborative care models of care delivery,<sup>71,72</sup> palliative care interventions,<sup>11</sup> and novel technology.<sup>73</sup> Evidence in support of antidepressant pharmacotherapy in cancer patients is far less robust. The few placebo-controlled trials conducted with depressed cancer patients have yielded mixed results.<sup>74-77</sup> Furthermore, only one of these placebo-controlled trials evaluated an antidepressant specifically in patients with advanced cancer.<sup>77</sup> Psychostimulants, used widely in the oncology and palliative care settings to treat fatigue, also have a role in the management of depression in patients with cancer. Homsí<sup>78</sup> reported a successful open trial of methylphenidate for depression in patients with advanced cancer.

Current clinical practice for the treatment of depression in patients with end-stage cancer is to institute empirical trials of antidepressants using a targeted symptom reduction approach. A personal or family history of depression and symptoms of excessive guilt, poor self-esteem, anhedonia, and ruminative thinking strengthen the argument for a medication trial. Selection of an antidepressant should be based on a number of considerations such as prior treatment response, an optimal match between the patient's target symptoms and the adverse-effect profile of the antidepressant (eg, using a sedating agent for the patient with anxiety and insomnia), and a low likelihood of drug-drug interactions (many chemotherapeutic and antifungal agents are metabolized by CYP 3A3/4 enzymes. Mirtazapine (Remeron) has several properties that make it a particularly attractive

antidepressant choice in patients with advanced cancer: it is sedating, causes weight gain, has few significant drug interactions, and is a partial 5HT-3 receptor antagonist (ie, has antiemetic properties). In line with this approach, the 5-HT-3 receptor blocking properties of mirtazapine and olanzapine have led some palliative care clinicians to recommend these agents as first-line medications for nausea.<sup>79</sup>

It is the rare exception for a patient with advanced cancer to have depressive symptoms in isolation. Patients typically have depressive symptoms alongside nausea, fatigue, pain, and perhaps cognitive impairment. For this reason, a targeted symptom reduction orientation is preferred over the practice of using medications only for patients who meet full diagnostic criteria for depression.

## Recent developments in end-of-life care

End-of-life care remains inadequate for many cancer patients. Despite major advances in palliative care research,<sup>80</sup> too many patients with advanced cancer have to contend with a health care system that is polarized between active (often "aggressive") treatment directed at cure (or prolongation of life)<sup>81-83</sup> or a focus on symptom management, comfort measures, and an explicit transition to hospice. In the United States, government-sponsored health care financing rules perpetuate this binary approach. Medicare pays for cancer treatments in patients with advanced disease, irrespective of the number of prior unsuccessful treatments or the likely effectiveness of additional treatments.<sup>82</sup> Additionally, patients can only receive the Medicare hospice benefit if a physician certifies they have 6 months or less to live and they agree to forgo active treatment.

Fortunately, recent studies have established important benefits of advance care planning and palliative care. Detering and colleagues<sup>84</sup> conducted a randomized trial comparing advance care planning to usual care with elderly hospitalized patients. In contrast to prior studies focused on completion rates of advance directives, the primary outcome of this study was whether a patient's end-of-life wishes were known and respected. Eighty-six percent of the patients in the advance care planning group had their end-of-life wishes known and followed, compared with 30% of the control patients. Furthermore, family members of patients who died reported significantly less distress, anxiety, and depression.<sup>84</sup>

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A similar and important palliative care intervention trial was recently reported from the Massachusetts General Hospital.<sup>11</sup> Patients with stage IV lung cancer were randomized to receive either usual care or a palliative care intervention. The intervention focused on assessment of physical and psychosocial symptoms, establishing goals of care, assisting with decision-making regarding treatment, and individualized coordination of care. Patients in the palliative care intervention group experienced improved quality of life, had less depression and physical symptom burden, and lived an average of 2.7 months longer than the usual care group despite receiving less aggressive care. Hopefully, studies such as these will shape policy decisions and health care funding mechanisms that promote a more rational and compassionate approach to end-of-life care, whether patients continue to receive active cancer treatment or not.<sup>85</sup>

## REFERENCES

1. Cancer Key Facts, World Health Organization. 2010. Available at: <http://www.who.int/mediacentre/factsheets/fs297/en/>.
2. Chochinov H, Wilson K, Enns M, et al. Prevalence of depression in the terminally ill: effects of diagnostic criteria and symptom threshold judgments. *Am J Psychiatry*. 1994;151:537-540.
3. Hotopf M, Chidgey J, Addington-Hall J, et al. Depression in advanced disease: a systematic review Part 1. Prevalence and case finding. *Palliative Med*. 2002;16:81-97.
4. Massie MJ. Prevalence of depression in patients with cancer. *JNCI Monographs*. 2004;57-71.
5. Shuster JL Jr, Breitbart W, Chochinov HM. Psychiatric aspects of excellent end-of-life care. *Psychosomatics*. 1999;40:1-4.
6. Bottomley A. Depression in cancer patients: a literature review. *Eur J Cancer Care*. 1998;7:181-191.
7. Keith GW, Harvey Max C, Merika Graham S, et al. Depression and anxiety disorders in palliative cancer care. *J Pain Symptom Management*. 2007;33:118-129.
8. Dy SM, Lorenz KA, Naeim A, et al. Evidence-based recommendations for cancer fatigue, anorexia, depression, and dyspnea. *J Clin Oncol*. 2008;26:3886-3895.
9. Ly KL, Chidgey J, Addington-Hall J, et al. Depression in palliative care: a systematic review. Part 2. Treatment. *Palliative Med*. 2002;16:279-284.
10. Chochinov HM, Hack T, Hassard T, et al. Dignity therapy: a novel psychotherapeutic intervention for patients near the end of life. *J Clin Oncol*. 2005;23:5520-5525.
11. Temel J, Greer J, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363:733-742.
12. Kissane DW, Grabsch B, Clarke DM, et al. Supportive-expressive group therapy: the transformation of existential ambivalence into creative living while enhancing adherence to anti-cancer therapies. *Psycho-Oncology*. 2004;13:755-768.
13. Bakitas M, Lyons KD, Hegel MT, et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer. *JAMA*. 2009;302:741-749.
14. Passik S, Dugan W, McDonald M, et al. Oncologists' recognition of depression in their patients with cancer. *J Clin Oncol*. 1998;16:1594-1600.
15. Breitbart W, Tremblay A, Gibson C. An open trial of olanzapine for the treatment of delirium in hospitalized cancer patients. *Psychosomatics*. 2002;43:175-182.
16. Peterson JF, Pun BT, Dittus RS, et al. Delirium and its motoric subtypes: a study of 614 critically ill patients. *J Am Geriatr Soc*. 2006;54:479-484.

## Conclusion

Depressive symptoms complicate end-of-life cancer care by contributing to physical and psychological morbidity. Depression may also be associated with increased mortality. Unfortunately, this treatable cause of suffering is frequently misdiagnosed and poorly treated in patients with cancer who are dying. In addition to traditional psychosocial and pharmacological treatments, several novel approaches to end-of-life care have been shown to result in robust improvement in depressive symptoms for patients with terminal cancer. These comprehensive and patient-centered interventions offer patients the incalculable benefits of less suffering and optimum communication with family, friends, and clinicians providing care for them at the end of life. □

17. Spiller JA, Keen JC. Hypoactive delirium: assessing the extent of the problem for inpatient specialist palliative care. *Palliative Med*. 2006;20:17-23.
18. Fang C-K, Chen H-W, Liu S-I, et al. Prevalence, detection and treatment of delirium in terminal cancer inpatients: a prospective survey. *Jpn J Clin Oncol*. 2008;38:56-63.
19. Bush SH, Bruera E. The assessment and management of delirium in cancer patients. *Oncologist*. 2009;14:1039-1049.
20. Meagher DJ, Moran M, Raju B, et al. Phenomenology of delirium: assessment of 100 adult cases using standardised measures. *Br J Psychiatry*. 2007;190:135-141.
21. Farrell KR, Ganzini L. Misdiagnosing delirium as depression in medically ill elderly patients. *Arch Intern Med*. 1995;155:2459-2464.
22. Breitbart W, Alici Y. Agitation and delirium at the end of life. *JAMA*. 2008;300:2898-2910.
23. Minagawa H, Uchitomi Y, Yamawaki S, et al. Psychiatric morbidity in terminally ill cancer patients: a prospective study. *Cancer*. 1996;78:1131-1137.
24. Breitbart W, Gibson C, Tremblay A. The delirium experience: delirium recall and delirium-related distress in hospitalized patients with cancer, their spouses/caregivers, and their nurses. *Psychosomatics*. 2002;43:183-194.
25. Tatsuya M, Tatsuo A, Masayuki I, et al. Terminal delirium: recommendations from bereaved families' experiences. *J Pain Symptom Management*. 2007;34:579-589.
26. Kawanishi C, Onishi H, Kato D, et al. Unexpectedly high prevalence of akathisia in cancer patients. *Palliative Supportive Care*. 2007;5:351-354.
27. Fleishman SB, Lavin MR, Sattler M, et al. Antiemetic-induced akathisia in cancer patients receiving chemotherapy. *Am J Psychiatry*. 1994;151:763-765.
28. Angelino A, Treisman G. Major depression and demoralization in cancer patients: diagnostic and treatment considerations. *Supportive Care Cancer*. 2001;9:344-349.
29. Clarke DM, Kissane DW. Demoralization: its phenomenology and importance. *Aust N Z J Psychiatry*. 2002;36:733-742.
30. Kissane DW, Wein S, Love A, et al. The Demoralization Scale: a report of its development and preliminary validation. *J Palliat Care*. 2004;20:269-276.
31. Chochinov HM, Wilson KG, Enns M, et al. Depression, hopelessness, and suicidal ideation in the terminally ill. *Psychosomatics*. 1998;39:366-370.
32. Weinberger MI, Roth AJ, Nelson CJ. Untangling the complexities of depression diagnosis in older cancer patients. *Oncologist*. 2009;14:60-66.
33. Trask PC. Assessment of depression in cancer patients. *JNCI Monographs*. 2004;80-92.
34. Teunissen SCCM, Wesker W, Kruitwagen C, et al. Symptom prevalence in patients with incurable cancer: a systematic review. *J Pain Symptom Management*. 2007;34:94-104.

### La depresión y los cuidados terminales para pacientes con cáncer

Los pacientes con cáncer y depresión experimentan más síntomas físicos, tienen una peor calidad de vida y una mayor probabilidad de tener pensamientos suicidas o deseos de acelerar la muerte que los pacientes con cáncer sin depresión. A pesar de la ubicuidad de los síntomas depresivos en los pacientes con cáncer al final de la vida, persisten preguntas críticas que no se han respondido en relación con la etiopatogenia, el diagnóstico y el tratamiento de la depresión en estos pacientes vulnerables. La farmacoterapia de la depresión en pacientes con cáncer avanzado debe estar guiada por una aproximación de cuidados paliativos orientada a la reducción de los síntomas, independiente de si el paciente cumple o no con los criterios diagnósticos para una depresión mayor. Las terapias de soporte más precoces e intensas para los pacientes con cáncer reducen el peso de los síntomas y pueden prolongar la vida para los pacientes con la enfermedad avanzada. Los ensayos clínicos orientados a los síntomas son necesarios para mejorar los cuidados del cáncer terminal.

### Dépression et soins de fin de vie pour les patients cancéreux

Les patients présentant un cancer et une dépression ont plus de symptômes physiques, une qualité de vie moins bonne, plus de pensées suicidaires ou de désir de fin de vie accélérée que les patients cancéreux non déprimés. Malgré l'omniprésence des symptômes dépressifs chez les patients cancéreux en fin de vie, certaines questions essentielles touchant l'étiopathogénie, le diagnostic et le traitement restent sans réponse chez ces patients vulnérables. Le traitement pharmacologique de la dépression chez des patients présentant un cancer évolué devrait s'effectuer selon une approche palliative centrée sur la diminution des symptômes, que le patient remplisse les critères diagnostiques d'une dépression majeure ou non. Une assistance plus précoce et plus intensive des patients cancéreux diminue la charge des symptômes et peut prolonger la vie des patients dont la maladie est évoluée. Des études cliniques orientées sur les symptômes sont nécessaires pour améliorer les soins de fin de vie au cours du cancer.

35. Kroenke K, Zhong X, Theobald D, et al. Somatic symptoms in patients with cancer experiencing pain or depression: prevalence, disability, and health care use. *Arch Intern Med.* 2010;170:1686-1694.
36. Frasure-Smith N, Lesperance F. Recent evidence linking coronary heart disease and depression. *Can J Psychiatry.* 2006;51:730-737.
37. Satin JR, Linden W, Phillips MJ. Depression as a predictor of disease progression and mortality in cancer patients. *Cancer.* 2009;115:5349-5361.
38. Hjerl K, Andersen EW, Keiding N, et al. Depression as a prognostic factor for breast cancer mortality. *Psychosomatics.* 2003;44:24-30.
39. Gathinji M, McGirt MJ, Attenello FJ, et al. Association of preoperative depression and survival after resection of malignant brain astrocytoma. *Surg Neurol.* 2009;71:299-303.
40. Chen DT, Miller FG, Rosenstein DL. Enrolling decisionally impaired adults in clinical research. *Med Care.* 2002;40:V20-V29.
41. Kim SYH, Karlawish JHT, Caine ED. Current state of research on decision-making competence of cognitively impaired elderly persons. *Am J Geriatr Psych.* 2002;10:151-165.
42. Misra S, Rosenstein D, Socherman R, et al. Bipolar mania and capacity to consent: Recommendations for investigators and IRBs. *Ethics Hum Res.* 2010;32:7-15.
43. Sullivan M, Youngner S. Depression, competence, and the right to refuse lifesaving medical treatment. *Am J Psychiatry.* 1994;151:971-978.
44. Grisso T, Appelbaum P. Comparison of standards for assessing patients' capacities to make treatment decisions. *Am J Psychiatry.* 1995;152:1033-1037.
45. Appelbaum PS, Grisso T, Frank E, et al. Competence of depressed patients for consent to research. *Am J Psychiatry.* 1999;156:1380-1384.
46. Elliott C. Caring about risks: are severely depressed patients competent to consent to research? *Arch Gen Psychiatry.* 1997;54:113-116.
47. Appelbaum PS. Assessment of patients' competence to consent to treatment. *N Engl J Med.* 2007;357:1834-1840.
48. Silveira MJ, Kim SYH, Langa KM. Advance directives and outcomes of surrogate decision making before death. *N Engl J Med.* 2010;362:1211-1218.
49. Bostwick JM, Masterson BJ. Psychopharmacological treatment of delirium to restore mental capacity. *Psychosomatics.* 1998;39:112-117.
50. Katz M, Abbey S, Rydall A, et al. Psychiatric consultation for competency to refuse medical treatment. A retrospective study of patient characteristics and outcome. *Psychosomatics.* 1995;36:33-41.
51. Abbey JG, Rosenfeld B, Pessin H, et al. Hopelessness at the end of life: the utility of the hopelessness scale with terminally ill cancer patients. *Br J Health Psychol.* 2006;11:173-183.
52. Akechi T, Okamura H, Yamawaki S, et al. Why do some cancer patients with depression desire an early death and others do not? *Psychosomatics.* 2001;42:141-145.
53. Yousaf U, Christensen ML, Engholm G, et al. Suicides among Danish cancer patients. 1971-1999. *Br J Cancer.* 2005;92:995-1000.
54. Allebeck P, Bolund C, Ringback G. Increased suicide rate in cancer patients. A cohort study based on the Swedish cancer-environment register. *J Clin Epidemiol.* 1989;42:611-616.
55. Misono S, Weiss NS, Fann JR, et al. Incidence of suicide in persons with cancer. *J Clin Oncol.* 2008;26:4731-4738.
56. Llorente MD, Burke M, Gregory GR, et al. Prostate cancer: a significant risk factor for late-life suicide. *Am J Geriatr Psych.* 2005;13:195-201.
57. Kendal WS. Suicide and cancer: a gender-comparative study. *Ann Oncol.* 2007;18:381-387.
58. van Leeuwen P, Schröder F. Risk factors: increased risk of suicide after prostate cancer diagnosis. *Nat Rev Urol.* 2010;7:369-370.
59. Hem E, Loge JH, Haldorsen T, et al. Suicide risk in cancer patients from 1960 to 1999. *J Clin Oncol.* 2004;22:4209-4216.
60. Robinson D, Renshaw C, Okello C, et al. Suicide in cancer patients in South East England from 1996 to 2005: a population-based study. *Br J Cancer.* 2009;101:198-201.

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61. Fallowfield L, Ratcliffe D, Jenkins V, et al. Psychiatric morbidity and its recognition by doctors in patients with cancer. *Br J Cancer*. 2001;84:1011-15.
62. Valente SM. Oncology Nurses' Knowledge of suicide evaluation and prevention. *Cancer Nursing*. 2010;33:290-295.
63. Walker J, Waters RA, Murray G, et al. Better off dead: suicidal thoughts in cancer patients. *J Clin Oncol*. 2008;26:4725-4730.
64. van der Lee ML, van der Bom JG, Swarte NB, et al. Euthanasia and depression: a prospective cohort study among terminally ill cancer patients. *J Clin Oncol*. 2005;23:6607-6612.
65. Breitbart W, Rosenfeld B, Pessin H, et al. Depression, hopelessness, and desire for hastened death in terminally ill patients with cancer. *JAMA*. 2000;284:2907-2911.
66. Ganzini L, Goy ER, Dobscha SK. Prevalence of depression and anxiety in patients requesting physicians' aid in dying: cross sectional survey. *BMJ*. 2008; 337.
67. Emanuel EJ, Fairclough DL, Emanuel LL. Attitudes and desires related to euthanasia and physician-assisted suicide among terminally ill patients and their caregivers. *JAMA*. 2000;284:2460-2468.
68. Muskin PR. The request to die. *JAMA*. 1998;279:323-328.
69. Foley KM. The relationships of pain and symptom management to patient requests for physician-assisted suicide. *J Pain Symptom Manage*. 1991;6:289-297.
70. Adler NE, Page AEK. *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs*. Institute of Medicine. Washington, DC: The National Academies Press: 2008.
71. Ell K, Xie B, Quon B, et al. Randomized controlled trial of collaborative care management of depression among low-income patients with cancer. *J Clin Oncol*. 2008;26:4488-4496.
72. Strong V, Waters R, Hibberd C, et al. Management of depression for people with cancer (SMaRT oncology 1): a randomised trial. *Lancet*. 2008;372:40-48.
73. Kroenke K, Theobald D, Wu J, et al. Effect of telecare management on pain and depression in patients with cancer. *JAMA*. 2010;304:163-171.
74. Costa D, Mogos I, Toma T. Efficacy and safety of mianserin in the treatment of depression of women with cancer. *Acta Psychiatrica Scandinavica*. 1985;72:85-92.
75. van Heeringen K, Zivkov M. Pharmacological treatment of depression in cancer patients. A placebo- controlled study of mianserin. *Br J Psychiatry*. 1996;169:440-443.
76. Razavi D, Allilaire JF, Smith M, et al. The effect of fluoxetine on anxiety and depression symptoms in cancer patients. *Acta Psychiatrica Scandinavica*. 1996; 94:205-210.
77. Fisch MJ, Loehrer PJ, Kristeller J, et al. Fluoxetine versus placebo in advanced cancer outpatients: a double-blinded trial of the Hoosier Oncology Group. *J Clin Oncol*. 2003;21:1937-1943.
78. Homsí J, Nelson KA, Sarhill N, et al. A phase II study of methylphenidate for depression in advanced cancer. *Am J Hospice Palliative Med*. 2001;18:403-407.
79. Kast RE, Foley KF. Cancer chemotherapy and cachexia: mirtazapine and olanzapine are 5-HT<sub>3</sub> antagonists with good anti-nausea effects. *Eur J Cancer Care*. 2007;16:351-354.
80. Ferris FD, Bruera E, Cherny N, et al. Palliative cancer care a decade later: accomplishments, the need, next steps, from the American Society of Clinical Oncology. *J Clin Oncol*. 2009;27:3052-3058.
81. Earle CC, Neville BA, Landrum MB, et al. Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol*. 2004;22:315-321.
82. Emanuel EJ, Young-Xu Y, Levinsky NG, et al. Chemotherapy use among medicare beneficiaries at the end of life. *Ann Intern Medicine*. 2003;138:639-643.
83. Earle CC, Landrum MB, Souza JM, et al. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *J Clin Oncol*. 2008;26:3860-3866.
84. Detering KM, Hancock AD, Reade MC, et al. The impact of advance care planning on end of life care in elderly patients: randomised controlled trial. *BMJ*. 2010;340.
85. Salz T, Brewer NT. Offering chemotherapy and hospice jointly: one solution to hospice underuse. *Medical Decision Making*. 2009;29:521-531.